PCT WORLD INTELLECTUAL PROPERTY ORGANIZATION
International Bureau

INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification 6 :
C07D 263/56, A01N 43/76, C07D 317/46, A01N 43/30, C07D 263/58, 277/64, A01N 43/78, C07D 307/79, 317/54, 333/64, 213/70, 213/61, 231/12

A1

(11) International Publication Number: **WO 95/25099**

(43) International Publication Date: 21 September 1995 (21.09.95)

(21) International Application Number: PCT/EP95/00950

(22) International Filing Date: 14 March 1995 (14.03.95)

(30) Priority Data:
9405229.7 17 March 1994 (17.03.94) GB

(71) Applicant *(for all designated States except US)*: RHONE-POULENC AGRICULTURE LTD. [GB/GB]; Fyfield Road, Ongar, Essex CM5 0HW (GB).

(72) Inventors; and
(75) Inventors/Applicants *(for US only)*: GEACH, Neil [GB/GB]; Rhone-Poulenc Agriculture Ltd., Fyfield Road, Ongar, Essex CM5 0HW (GB). HAWKINS, David, William [GB/GB]; Rhone-Poulenc Agriculture Ltd., Fyfield Road, Ongar, Essex CM5 0HW (GB). PEARSON, Christopher, John [GB/GB]; Rhone-Poulenc Agriculture Ltd., Fyfield Road, Ongar, Essex CM5 0HW (GB). SMITH, Philip, Henry, Gaunt [GB/GB]; Rhone-Poulenc Agriculture Ltd., Fyfield Road, Ongar, Essex CM5 0HW (GB). WHITE, Nicolas [GB/GB]; Rhone-Poulenc Agriculture Ltd., Fyfield Road, Ongar, Essex CM5 0HW (GB).

(74) Agent: RHONE-POULENC AGROCHIMIE; DPI - Brachotte, Charles, Boîte postale 9163, F-69263 Lyon Cédex 09 (FR).

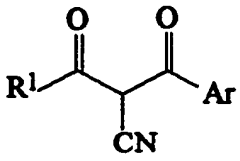
(81) Designated States: AM, AU, BB, BG, BR, BY, CA, CN, CZ, EE, FI, GE, HU, KG, KP, KR, KZ, LK, LR, LT, LV, MD, MG, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TJ, TT, UA, UG, US, UZ, VN, European patent (AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG), ARIPO patent (KE, MW, SD, SZ, UG).

Published
With international search report.

(54) Title: 2-CYANO-1,3-DIONE DERIVATIVES USEFUL AS HERBICIDES

(57) Abstract

The invention relates to 2-cyano-1,3-dione derivatives of formula (I), wherein R^1 and Ar are as defined in the description, and to their use as herbicides.



(I)

FOR THE PURPOSES OF INFORMATION ONLY

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

AT	Austria	**GB**	United Kingdom	**MR**	Mauritania
AU	Australia	**GE**	Georgia	**MW**	Malawi
BB	Barbados	**GN**	Guinea	**NE**	Niger
BE	Belgium	**GR**	Greece	**NL**	Netherlands
BF	Burkina Faso	**HU**	Hungary	**NO**	Norway
BG	Bulgaria	**IE**	Ireland	**NZ**	New Zealand
BJ	Benin	**IT**	Italy	**PL**	Poland
BR	Brazil	**JP**	Japan	**PT**	Portugal
BY	Belarus	**KE**	Kenya	**RO**	Romania
CA	Canada	**KG**	Kyrgystan	**RU**	Russian Federation
CF	Central African Republic	**KP**	Democratic People's Republic of Korea	**SD**	Sudan
CG	Congo			**SE**	Sweden
CH	Switzerland	**KR**	Republic of Korea	**SI**	Slovenia
CI	Côte d'Ivoire	**KZ**	Kazakhstan	**SK**	Slovakia
CM	Cameroon	**LI**	Liechtenstein	**SN**	Senegal
CN	China	**LK**	Sri Lanka	**TD**	Chad
CS	Czechoslovakia	**LU**	Luxembourg	**TG**	Togo
CZ	Czech Republic	**LV**	Latvia	**TJ**	Tajikistan
DE	Germany	**MC**	Monaco	**TT**	Trinidad and Tobago
DK	Denmark	**MD**	Republic of Moldova	**UA**	Ukraine
ES	Spain	**MG**	Madagascar	**US**	United States of America
FI	Finland	**ML**	Mali	**UZ**	Uzbekistan
FR	France	**MN**	Mongolia	**VN**	Viet Nam
GA	Gabon				

2-CYANO-1,3-DIONE DERIVATIVES USEFUL AS HERBICIDES

TECHNICAL FIELD

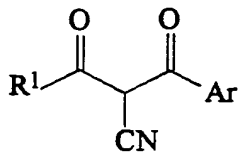
This invention relates to novel 2-cyano-1,3-dione derivatives, compositions containing them, processes for their preparation and their use as herbicides.

BACKGROUND ART

European Patent Publication Nos. 0496630 and 0496631 disclose certain 1-phenyl-2-cyano-1,3-dione derivatives possessing herbicidal properties. European Patent Publication No 0213892 discloses herbicidally active enols.

DESCRIPTION OF THE INVENTION

The present invention provides 2-cyano-1,3-dione derivatives of formula I:



(I)

wherein:

Ar represents a monocyclic or fused bicyclic heterocyclic system Het having a heterocyclic first ring and an optional second heterocyclic or carbocyclic ring, the second ring when present being fused to the first ring, the first ring having from 1 to 4 hetero ring atoms and from 4 to 7 total ring atoms, the hetero ring atoms preferably being selected from oxygen, nitrogen and sulphur, the first ring being aromatic or non-aromatic and being optionally substituted by from 1 to 4 R^2 groups which may be the same or different, the second ring being optionally substituted by from 1 to 4 R^2 groups which may be the same or different;

R^1 represents a cycloalkyl group containing from three to six carbon atoms optionally substituted by one or more groups selected from R^4, $-CO_2R^4$, $-SR^4$, halogen and $-OR^4$;

R^2 represents:-

a halogen atom,

a straight- or branched- chain alkyl group containing from one to six carbon atoms which is substituted by a group $-OR^4$; or

a group selected from -OH, R^4, $-SR^5$, $-SOR^5$, $-SO_2R^5$, $-O-SO_2R^5$, $-CO_2R^4$, $-COR^4$, $-OR^5$, $-NR^6R^7$, $-N(R^8)SO_2R^5$, nitro, cyano, $-O(CH_2)_m-OR^4$, $-(-CR^9R^{10}-)_t-S(O)_pR^5$ and $-NR^{11}R^{12}$;

when the first and/or second ring of Het is non-aromatic, then R^2 may also represent =O, =S, cyclic ketal or cyclic thioketal;

R^4 represents a straight- or branched- chain alkyl group containing from one to six carbon atoms which is optionally substituted by one or more halogen atoms;

R^5 represents:-

a group R^4 or

phenyl optionally substituted by from one to five groups selected from halogen, R^4, $-CO_2R^4$, $-COR^4$, $-OR^4$, nitro, cyano and $-O(CH_2)_m-OR^4$;

R^6 and R^7, which may be the same or different, each represent the hydrogen atom or a straight- or branched- chain alkyl group containing from one to six carbon atoms which is optionally substituted by one or more halogen atoms;

m represents an integer from one to three;

R^8 represents:-

the hydrogen atom;

a straight- or branched-chain alkyl, alkenyl or alkynyl group containing up to ten carbon atoms which is optionally substituted by one or more halogen atoms;

R^9 and R^{10}, which may be the same or different, each represents:

the hydrogen atom; a straight- or branched-chain alkyl group containing up to 6 carbon atoms which is optionally substituted by one or more halogen atoms; or phenyl optionally substituted by from one to five groups which may be the same or different selected from halogen, R^4, $-CO_2R^4$, $-COR^4$, $-OR^4$, nitro, cyano and $-O(CH_2)_m-OR^4$;

p is zero, 1 or 2; t represents an integer from one to three;

R^{11} represents $-COR^4$ or $-CO_2R^4$;

R^{12} represents:-

the hydrogen atom;

a straight- or branched- chain alkyl group containing up to six carbon atoms optionally substituted by one or more halogen atoms;

or a cycloalkyl group containing from three to six carbon atoms;

enolic tautomeric forms thereof, and agriculturally acceptable salts or metal complexes thereof, which possess valuable herbicidal properties.

These compounds possess valuable herbicidal properties, in particular in their control of economically important weed species such as Echinochloa crus-galli (Barnyard grass) and Amaranthus retroflexus (Pigweed).

Compounds of formula I may exist in enolic tautomeric forms that may give rise to geometric isomers around the enolic double bond. Furthermore, in certain cases the substituents R^1, R^2, R^4, R^5, R^6, R^7, R^8, R^9, R^{10}, R^{11} and R^{12} contribute to optical isomerism and/or stereoisomerism. All such forms are embraced by the present invention.

By the term "agriculturally acceptable salts" is meant salts the cations of which are known and accepted in the art for the formation of salts for agricultural or horticultural use. Preferably the salts are water-soluble. Suitable acid addition salts formed by compounds of formula I include salts with inorganic acids, for example hydrochlorides, sulphates, phosphates and nitrates and salts with organic acids, for example acetic acid.

By the term "metal complexes" is meant compounds in which one or both of the oxygen atoms of the 1,3-dione act as chelating agents to a metal cation. Examples of such cations include zinc, manganese, cupric, cuprous, ferric, ferrous, titanium and aluminium.

It will be understood in the definition of Het, where the first heterocyclic and/or the second ring contains a sulphur atom in the ring, the sulphur atom may be in the form of a group -SO- or $-SO_2-$.

Where R^2 represents cyclic ketal or cyclic thioketal preferably the ketal or thioketal ring contains 5 or 6 ring members.

Examples of the group Het include:

thienyl, furyl, pyrrolyl and their benzo-fused analogues;

oxazinyl, thiazinyl, pyrazinyl, pyrimidinyl, pyridazinyl and their

benzo-fused analogues;

thiazolyl, oxazolyl, imidazolyl and their benzo-fused analogues;

pyrazolyl, isoxazolyl, isothiazolyl and their benzo-fused analogues;

oxadiazolyl, thiadiazolyl, triazolyl and, where appropriate, their benzo-fused analogues;

pyridinyl, pyranyl, thiinyl and their benzo-fused analogues;

oxadiazinyl, thiadiazinyl, triazinyl and, where appropriate, their benzo-fused analogues;

tetrazolyl, piperidinyl, morpholinyl and piperazinyl.

Preferably R^1 represents a cyclopropyl group optionally substituted by a group R^4 (especially where R^4 is alkyl). More preferably R^1 represents 1-methylcyclopropyl or, most preferably, cyclopropyl.

In one aspect compounds of formula (I) in which Ar represents an optionally substituted fused bicyclic heterocyclic system having a heterocyclic first ring and a second carbocyclic ring (e.g. a benzene ring) are preferred. Compounds in which Ar represents optionally substituted 1,3-benzodioxole, benzo[b]thiophene, benzoxazolinone, benzoxazole or benzo[b]furan are particularly preferred.

Where Het is a fused bicyclic heterocyclic system either the heterocyclic first ring or the second ring may be attached to the carbonyl group of the 2-cyano-1,3-dione.

Compounds of formula I in which Ar represents optionally substituted pyridyl, pyrazolyl or thienyl are also preferred.

Compounds of formula (I) in which R^2 represents a halogen atom or a group selected from $-SR^5$, $-SOR^5$, $-SO_2R^5$, $-CH_2S(O)_pR^5$, $-CO_2R^4$ and $-OR^5$ are also preferred.

Compounds in which R^5 represents a straight- or branched-chain alkyl group containing from one to six carbon atoms are also preferred, most preferably methyl.

Preferably Ar represents a group Het which is optionally substituted by from one to three groups R^2.

Particularly important compounds of formula (I) because of their herbicidal activity include the following:

1. 2-cyano-3-cyclopropyl-1-(2,2-difluoro-1,3-benzodioxol-

4-yl)propan-1,3-dione;

2. 1-(2-t-butyl-4-chlorobenzoxazol-7-yl)-2-cyano-3-cyclopropylpropan-1,3-dione;

3. 2-cyano-3-cyclopropyl-1-(2,2-difluoro-4-methylsulphonyl-1,3-benzodioxol-5-yl)propan-1,3-dione;

4. 2-cyano-3-cyclopropyl-1-(4-fluoro-3-methyl-1,3-benzoxazolin-2-one-7-yl)propan-1,3-dione;

5. 1-(2-t-butyl-4-methylthiobenzoxazol-7-yl)-2-cyano-3-cyclopropylpropan-1,3-dione;

6. 2-cyano-3-cyclopropyl-1-(2,3-dihydrobenzo[b]furan-5-yl)propan-1,3-dione;

7. 2-cyano-3-cyclopropyl-1-(1,3-benzodioxol-5-yl)propan-1,3-dione;

8. 1-(4-chloro-3-methoxybenzo[b]thien-5-yl)-2-cyano-3-cyclopropylpropan-1,3-dione;

9. 2-cyano-3-cyclopropyl-1-(5-methylthiopyrid-2-yl)propan-1,3-dione;

10. 1-(3-chloro-5-trifluoromethylpyrid-2-yl)-2-cyano-3-cyclopropylpropan-1,3-dione;

11. 2-cyano-3-cyclopropyl-1-(2-methylthiopyrid-3-yl)propan-1,3-dione;

12. 2-cyano-3-cyclopropyl-1-(1-ethyl-3-trifluoromethyl-pyrazol-4-yl)propan-1,3-dione;

13. 2-cyano-3-cyclopropyl-1-(4-methylsulphonyl-1,3-benzodioxol-5-yl)propan-1,3-dione;

14. 2-cyano-3-cyclopropyl-1-(4-methylthio-1,3-benzodioxol-5-yl)propan-1,3-dione; and

15. 1-(1,3-benzodioxol-4-yl)-2-cyano-3-cyclopropylpropan-1,3-dione.

The numbers 1 to 15 are assigned to these compounds for reference and identification hereinafter

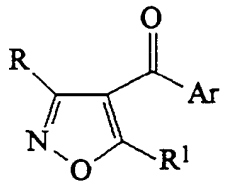
Compounds of formula (I) may be prepared by the application or adaptation of known methods (i.e. methods heretofore used or described in the literature), for example as hereinafter described.

In the following description where symbols appearing in formulae are not specifically defined, it is to be understood that they

are "as hereinbefore defined" in accordance with the first definition of each symbol in the specification.

It is to be understood that in the descriptions of the following processes the sequences may be performed in different orders, and that suitable protecting groups may be required to achieve the compounds sought.

According to a feature of the present invention compounds of formula (I) may be prepared by the reaction of a compound of formula(II):



(II)

wherein R^1 and Ar are as hereinbefore defined and R represents the hydrogen atom or an ester, with a base. Preferably R represents the hydrogen atom. Preferred bases include alkali or alkaline earth metal hydroxides or alkoxides such as sodium ethoxide, or organic bases such as triethylamine. The reaction is generally performed at a temperature from room temperature to the reflux temperature of the mixture.

According to a further feature of the present invention, compounds of formula (I) may also be prepared by the reaction of an acid chloride of formula (III):

$$ArC(O)Cl \qquad (III)$$

wherein Ar is as hereinbefore defined, with a beta-ketonitrile of formula(IV):

$$R^1C(O)CH_2CN \qquad (IV)$$

wherein R^1 is as hereinbefore defined. The reaction is generally performed in the presence of a base in a solvent or solvent mixture. Suitable bases include metal hydrides, hydroxides or alkoxides (e.g. sodium or lithium hydride, sodium hydroxide, potassium hydroxide, magnesium ethoxide or magnesium methoxide), and organic bases such as triethylamine. Suitable solvents include for example tetrahydrofuran; hydrocarbons such as toluene; or halogenated hydrocarbons such as dichloromethane.

The reaction is generally performed at a temperature from 0°C to reflux temperature.

According to a further feature of the present invention, compounds of formula (I) may also be prepared by the reaction of an acid chloride of formula (V):

$$R^1COCl \qquad (V)$$

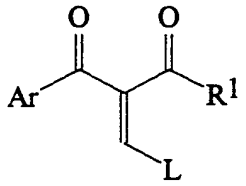
wherein R^1 is as hereinbefore defined, with a beta-ketonitrile of formula (VI):

$$ArC(O)CH_2CN \qquad (VI)$$

wherein Ar is as hereinbefore defined. The reaction is generally performed in the presence of a base in a solvent or solvent mixture. Suitable bases include metal hydrides, hydroxides or alkoxides (e.g. sodium or lithium hydride, sodium hydroxide, potassium hydroxide, magnesium ethoxide or magnesium methoxide), and organic bases such as triethylamine. Suitable solvents include for example tetrahydrofuran; hydrocarbons such as toluene; or halogenated hydrocarbons such as dichloromethane. The reaction is generally performed at a temperature from 0°C to reflux temperature.

Intermediates in the preparation of compounds of formula I may be prepared by the application or adaptation of known methods, for example as described hereinafter.

Intermediates of formula (II) in which R represents hydrogen may be prepared by the reaction of a compound of formula (VII):

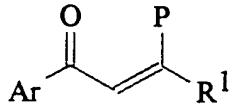


(VII)

wherein L is a leaving group and Ar and R^1 are as hereinbefore defined, with a salt of hydroxylamine. Hydroxylamine hydrochloride is generally preferred. Preferably L is ethoxy or N,N-dimethylamino. The reaction is generally carried out in a solvent such as ethanol or acetonitrile, optionally in the presence of a base or acid acceptor such as triethylamine or sodium acetate.

Intermediates of formula (II) wherein R represents an ester

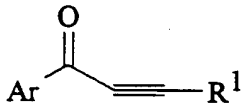
may be prepared by the reaction of a compound of formula (VIII)



(VIII)

wherein Ar and R^1 are as hereinbefore defined and P is a leaving group, with a compound of formula RC(X)=NOH wherein R is an ester and X is a halogen atom. Generally X is chlorine or bromine and P represents N,N-dialkylamino. The reaction is generally performed in an inert solvent such as toluene or dichloromethane either in the presence of a base such as triethylamine or a catalyst such as a 4 Angstrom molecular sieve or fluoride ion.

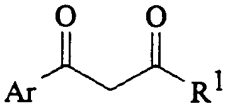
Intermediates of formula (II) in which R represents an ester may be prepared by the reaction of a compound of formula (IX):



(IX)

wherein Ar and R^1 are as hereinbefore defined, with a compound of formula RC(X)=NOH wherein R is an ester and X is as hereinbefore defined. The reaction is generally performed in an inert solvent such as toluene or dichloromethane optionally in the presence of a base such as triethylamine or a catalyst such as a 4 Angstrom molecular sieve or fluoride ion. The reaction can be carried out at a temperature between room temperature and the reflux temperature of the mixture.

Intermediates of formula (II) in which R represents an ester may also be prepared by the reaction of the salt of a compound of formula (X):

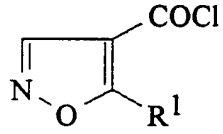


(X)

wherein Ar and R^1 are as hereinbefore defined, with a compound of formula RC(X)=NOH wherein R is an ester and X is as hereinbefore defined. Preferred salts include sodium or magnesium salts. The reaction may be performed in an inert

solvent such as dichloromethane or acetonitrile at a temperature between room temperature and the reflux temperature of the mixture.

Intermediates of formula (II) in which R represents hydrogen may be prepared by the reaction of a compound of formula (XI):



(XI)

wherein R^1 is as hereinbefore defined, with a compound of formula Ar-H, wherein Ar is as hereinbefore defined. The reaction is generally performed in the presence of a Lewis acid catalyst such as aluminium trichloride, in an inert solvent at a temperature from 0°C to the reflux temperature of the mixture.

Intermediates of formula (VII) may be prepared by the reaction of the corresponding compound of formula (X) with either a trialkyl orthoformate such as triethyl orthoformate or a dimethylformamide dialkylacetal such as N,N-dimethylformamide dimethyl acetal. The reaction with triethyl orthoformate is generally carried out in the presence of acetic anhydride at the reflux temperature of the mixture and the reaction with N,N-dimethyl formamide dialkyl acetal is carried out optionally in the presence of an inert solvent at a temperature from room temperature to the reflux temperature of the mixture.

Intermediates of formula (VIII) may be prepared by the reaction of a compound of formula (XII):

$$CH_2=C(P)R^1 \qquad \text{(XII)}$$

wherein R^1 and P are as hereinbefore defined, with an acid chloride of formula (III) as hereinbefore defined. The reaction is generally carried out in the presence of an organic base such as triethylamine in an inert solvent such as toluene or dichloromethane at a temperature between -20°C and room temperature.

Intermediates of formula (IX) may be prepared by the metallation of the appropriate acetylene of formula (XIII):

$$R^1C{\equiv}CH \qquad \text{(XIII)}$$

wherein R^1 is as hereinbefore defined, followed by reaction of the metal salt thus obtained with an acid chloride of formula (III) as

hereinbefore defined. The metallation is generally performed using n-butyl lithium in an inert solvent such as ether or tetrahydrofuran at a temperature from -78°C to 0°C. The subsequent reaction with the acid chloride is carried out in the same solvent at a temperature between -78°C and room temperature.

Those skilled in the art will appreciate that some compounds of formula I may be prepared by the inter-conversion of other compounds of formula I and such inter-conversions constitute yet more features of the present invention. Examples of such inter-conversions are hereafter described.

According to a further feature of the present invention compounds in which R^2 represents $-SOR^5$ or $-SO_2R^5$ may be prepared by the oxidation of the sulphur atom of the corresponding compound in which R^2 represents $-SR^5$ or $-SOR^5$. According to a further feature of the invention compounds of formula (I) in which a ring member of the group Het is -SO- or $-SO_2-$ may be prepared by the oxidation of the ring sulphur atom of the corresponding compound of formula (I). The oxidation of the sulphur atom is generally carried out using for example 3-chloroperoxy-benzoic acid in an inert solvent such as dichloromethane at a temperature from -40°C to room temperature.

Compounds of formulae (III), (IV), (V), (VI), (X), (XI), (XII)and (XIII) are known or may be prepared by the application and adaptation of known methods.

Agriculturally acceptable salts and metal complexes of compounds of formula (I) may be prepared by known methods.

The following examples illustrate the preparation of compounds of formula (I). In the present specification b.p. means boiling point, m.p. means melting point. Where the letters NMR appear, the characteristics of the proton nuclear magnetic resonance spectrum follow. Unless otherwise specified the percentages are by weight.

Example 1

Sodium methoxide (0.049g) was added to a stirred suspension of 4-(4-chloro-3-methoxybenzo[b]thien-5-oyl)-5-cyclopropylisoxazole (0.2g) in methanol (5 ml) at room temperature. After 4 hours

additional sodium methoxide (0.049g) was added and stirring maintained for 18 hours. The mixture was poured onto water, acidified (2N hydrochloric acid) and extracted (ether). The solution was dried (magnesium sulphate), evaporated and titurated with ether to give 1-(4-chloro-3-methoxybenzo[b]thien-5-yl)-2-cyano-3-cyclopropylpropan-1,3-dione (compound 8, 0.15g) as an orange solid, m.p. 165-168°C.

Similarly prepared was 2-cyano-3-cyclopropyl-1-(2-methylthiopyrid-3-yl)propan-1,3-dione (compound 11), m.p. 75-77.5°C, using sodium ethoxide, prepared from a mixture of 5-cyclopropyl-4-(2-methylthiopyridin-3-oyl)isoxazole and 4-cyclopropylcarbonyl-5-(2-methylthiopyrid-3-yl)isoxazole.

Example 2

Triethylamine (dry, 1.0 ml) was added to a stirred solution of 4-(1,3-benzodioxol-5-oyl)-5-cyclopropylisoxazole (1.73g) in dry dichloromethane. After 18 hours at room temperature the solution was washed in turn with water, dilute hydrochloric acid and water. The solution was dried (magnesium sulphate), evaporated and chromatographed on silica gel eluting with hexane/ethyl acetate to give 2-cyano-3-cyclopropyl-1-(1,3-benzodioxol-5-yl)propan-1,3-dione (compound 7, 1.0g) as a yellow solid, m.p. 78-80°C.

By proceeding in a similar manner the following compounds were prepared:

1-(2-t-butyl-4-methylthiobenzoxazol-7-yl)-2-cyano-3-cyclopropylpropan-1,3-dione (compound 5) as a yellow solid, m.p. 124-125°C.

2-cyano-3-cyclopropyl-1-(4-fluoro-3-methyl-2-oxo-1,3-benzoxazolin-7-yl)propan-1,3-dione (compound 4) as a cream solid NMR($CDCl_3$) 1.05(2H,m), 1.1(2H,m), 2.1(1H,m), 3.3(3H,s), 6.85(1H,t), 7.25(1H,dd), 10.3(1H,brs).

2-cyano-3-cyclopropyl-1-(2,2-difluoro-4-methylsulphonyl-1,3-benzodioxol-5-yl)propan-1,3-dione(compound 3) as a cream solid, m.p. 151-152°C.

1-(2-t-butyl-4-chlorobenzoxazol-7-yl)-2-cyano-3-cyclopropylpropan-1,3-dione (compound 2) as a pink solid, m.p. 99-101°C, from 5-(2-t-butyl-4-chlorobenzoxazol-7-yl)-4-

cyclopropylcarbonylisoxazole.

2-cyano-3-cyclopropyl-1-(5-methylthiopyrid-2-yl)propan-1,3-dione (compound 9), m.p. 126-128°C, from 4-cyclopropylcarbonyl-5-(methylthiopyrid-2-yl)isoxazole.

1-(3-chloro-5-trifluoromethylpyrid-2-yl)-2-cyano-3-cyclopropylpropan-1,3-dione (compound 10), m.p. 100-101.5°C, from 4-cyclopropylcarbonyl-5-(3-chloro-5-trifluoromethylpyrid-2-yl)isoxazole.

2-cyano-3-cyclopropyl-1-(2,3-dihydrobenzo[b]furan-5-yl)propan-1,3-dione (compound 6), m.p. 81-82°C, from 4-cyclopropylcarbonyl-5-(2,3-dihydrobenzo[b]furan-5-yl)isoxazole.

2-cyano-3-cyclopropyl-1-(2,2-difluoro-1,3-benzodioxol-4-yl)propan-1,3-dione (compound 1), m.p. 114-115°C, from 4-cyclopropylcarbonyl-5-(2,2-difluoro-1,3-benzodioxol-4-yl)isoxazole.

2-cyano-3-cyclopropyl-1-(4-methylsulphonyl-1,3-benzodioxol-5-yl)propan-1,3-dione (compound 13) as a solid, m.p. 208 - 210°C.

2-cyano-3-cyclopropyl-1-(4-methylthio-1,3-benzodioxol-5-yl)propan-1,3-dione (compound 14) as a solid, m.p. 90 - 92°C.

1-(1,3-benzodioxol-4-yl)-2-cyano-3-cyclopropylpropan-1,3-dione (compound 15) as a solid, m.p. 79 - 80°C.

Example 3

A solution of 4-(3-cyclopropyl-2-dimethylaminomethylene-1,3-dioxoprop-1-yl)-1-ethyl-3-trifluoromethylpyrazole (1.47g), sodium acetate (anhydrous 0.4g) and hydroxylamine hydrochloride (0.34g) was stirred overnight at room temperature in ethanol. The mixture was evaporated to dryness and purified by chromatography on silica gel eluting with hexane/ethyl acetate to give 2-cyano-3-cyclopropyl-1-(1-ethyl-3-trifluoromethylpyrazol-4-yl)propan-1,3-dione (compound 12, 0.39g) as a white solid, m.p. 135-137°C.

Reference Example 1

A solution of 5-cyclopropyl-4-(2,2-difluoro-4-methylsulphinyl-1,3-benzodioxol-5-oyl)isoxazole (1.0g) in dichloromethane was stirred with m-chloroperbenzoic acid (55%, 1.33g) for 5 hours, then washed in turn with sodium metabisulphite solution, saturated sodium bicarbonate solution and with water. The solution was dried

(magnesium sulphate), evaporated to dryness and the residue recrystallised from toluene/cyclohexane to give 5-cyclopropyl-4-(2,2-difluoro-4-methylsulphonyl-1,3-benzodioxol-5-oyl)isoxazole (0.94g) as a colourless solid, m.p. 162-163°C.

By proceeding in a similar manner the folllowing compounds were prepared:

5-cyclopropyl-4-(2,2-difluoro-4-methylsulphinyl-1,3-benzodioxol-5-oyl)isoxazole as a colourless solid, m.p. 162-164°C.

5-cyclopropyl-4-(4-methylsulphonyl-1,3-benzodioxol-5-oyl)isoxazole as a peach solid, m.p. 178 - 180°C.

Reference Example 2

A solution of 3-cyclopropyl-2-(dimethylamino)methylene-1-(2,2-difluoro-1,3-benzodioxol-4-yl)propan-1,3-dione (10.0g) in ethanol was stirred overnight with hydroxylamine hydrochloride (2.37g). Water was added and the mixture extracted with ethyl acetate, washed (brine), dried (sodium sulphate) and evaporated. Purification by chromatography on silica gel eluting with ethyl acetate/cyclohexane (1:25) gave 4-cyclopropylcarbonyl-5-(2,2-difluoro-1,3-benzodioxol-4-yl)isoxazole (2.48g) as a white solid, m.p. 92-95°C.

By proceeding in a similar manner the following compounds were prepared:

A mixture of 5-cyclopropyl-4-(2-methylthiopyridin-3-oyl)isoxazole and 4-cyclopropylcarbonyl-5-(2-methylthiopyrid-3-yl)isoxazole used directly in the next stage.

4-cyclopropylcarbonyl-5-(5-methylthiopyrid-2-yl)isoxazole, m.p. 103-104°C.

5-cyclopropyl-4-(4-fluoro-3-methyl-2-oxo-1,3-benzoxazol-7-oyl)-isoxazole as an orange gum.

4-cyclopropylcarbonyl-5-(3-chloro-5-trifluoromethylpyrid-2-yl)isoxazole, m.p. 89-91°C.

5-cyclopropyl-4-(4-methylthio-1,3-benzodioxol-5-oyl)isoxazole as a yellow gum, NMR ($CDCl_3$) d 1.2(2H,m), 1.3(2H,m), 2.4(3H,s), 2.7(1H,m), 6.1(2H,s), 6.8(1H,d), 7.0(1H,d), 8.2(1H,s).

5-cyclopropyl-4-(1,3-benzodioxol-4-oyl)isoxazole, m.p. 68 - 70°C.

Reference Example 3

A solution of 2-t-butyl-4-chloro-7-(3-cyclopropyl-2-ethoxymethylene-1,3-dioxoprop-1-yl)benzoxazole (3.3g), hydroxylamine hydrochloride (0.74g) and anhydrous sodium acetate (0.73g) in ethanol was stirred for 2 hours. Water was added and the mixture extracted with ether. The extract was washed with water, dried (magnesium sulphate) and evaporated. Purification by chromatography on silica gel eluting with hexane/ethyl acetate gave 5-(2-t-butyl-4-chlorobenzoxazol-7-yl)-4-cyclopropylcarbonylisoxazole, as a yellow gum, NMR ($CDCl_3$) δ 0.95(2H,m), 1.24(2H,m), 1.49(9H,s), 7.47(1H,d), 7.80(1H,d), 8.79(1H,s).

By proceeding in a similar manner the following compounds were prepared:

5-cyclopropyl-4-(2,2-difluoro-4-methylthio-1,3-benzodioxol-5-oyl)isoxazole as an orange gum, NMR ($CDCl_3$) δ 1.25(2H,m), 1.35(2H,m), 2.6(3H,s), 2.75(1H,m), 7.05(1H,d), 7.23(1H,d), 8.25(1H,s).

4-(2-t-butyl-4-methylthio-benzoxazol-7-oyl)-5-cyclopropylisoxazole, as a yellow glass, used directly in the next stage.

4-cyclopropylcarbonyl-5-(2,3-dihydrobenzo[b]furan-5-yl)isoxazole.

4-(1,3-benzodioxol-5-oyl)-5-cyclopropylisoxazole, as an orange gum used directly in the next stage.

4-(4-chloro-3-methoxybenzo[b]thien-5-oyl)-5-cyclopropylisoxazole, as a yellow gum NMR ($CDCl_3$) δ 1.23(2H,m), 1.34(2H,m), 2.67(1H,m), 4.0(3H,s), 6.5(1H,s), 7.3(1H,d), 7.73(1H,d), 8.17(1H,s).

Reference Example 4

A solution of 4-(3-cyclopropyl-1,3-dioxoprop-1-yl)-2,2-difluoro-1,3-benzodioxole (12.0g) in dry toluene was treated with N,N-dimethylformamide dimethyl acetal and the mixture stirred overnight. After evaporation in vacuo and re-evaporation after addition of toluene the residue was recrystallised from cyclohexane-ethanol to give 4-(3-cyclopropyl-2-dimethylaminomethylene-1,3-dioxoprop-1-yl)-2,2-difluoro-1,3-benzodioxole (6.5g) as a pale yellow solid, m.p. 118-119°C.

By proceeding in a similar manner the following compounds were prepared:

7-(3-cyclopropyl-2-dimethylaminomethylene-1,3-dioxoprop-1-yl)-4-fluoro-3-methyl-1,3-benzoxazol-2-one, from 7-(3-cyclopropyl-1,3-dioxoprop-1-yl)-4-fluoro-1,3-benzoxazol-2-one. N-Methylation occurred during this reaction.

2-(3-cyclopropyl-2-dimethylaminomethylene-1,3-dioxoprop-1-yl)-5-methylthiopyridine.

3-(3-cyclopropyl-2-dimethylaminomethylene-1,3-dioxoprop-1-yl)-2-methylthiopyridine.

4-(3-cyclopropyl-2-dimethylaminomethylene-1,3-dioxoprop-1-yl)-1-ethyl-3-trifluoromethylpyrazole.

3-chloro-2-(3-cyclopropyl-2-dimethylaminomethylene-1,3-dioxoprop-1-yl)-5-trifluoromethylpyridine.

4-(3-cyclopropyl-2-dimethylaminomethylene-1,3-dioxoprop-1-yl)-2,2-difluoro-7-methylthio-1,3-benzodioxole.

4-(3-cyclopropyl-2-dimethylaminomethylene-1,3-dioxoprop-1-yl)-3-methylthiopyridine.

5-(3-cyclopropyl-2-dimethylaminomethylene-1,3-dioxoprop-1-yl)-4-methylthio-1,3-benzodioxole.

4-(3-cyclopropyl-2-dimethylaminomethylene-1,3-dioxoprop-1-yl)-1,3-benzodioxole.

Reference Example 5

A mixture of 5-(3-cyclopropyl-1,3-dioxoprop-1-yl)-2,3-dihydrobenzo[b]furan (2.9g), triethyl orthoformate (6.2 ml) and acetic anhydride (50 ml) was stirred at reflux for 3 hours. The mixture was evaporated to dryness and re-evaporated after addition of toluene, to give 5-(3-cyclopropyl-2-ethoxymethylene-1,3-dioxoprop-1-yl)-2,3-dihydrobenzo[b]furan (4.17g).

By proceeding in a similar manner the following compounds were prepared:

5-(3-cyclopropyl-2-ethoxymethylene-1,3-dioxoprop-1-yl)-1,3-benzodioxole.

2-t-butyl-4-chloro-7-(3-cyclopropyl-2-ethoxymethylene-1,3-dioxoprop-1-yl)benzoxazole as an orange oil.

5-(3-cyclopropyl-2-ethoxymethylene-1,3-dioxoprop-1-yl)-2,2-difluoro-4-methylthio-1,3-benzodioxole.

2-t-butyl-7-(3-cyclopropyl-2-ethoxymethylene-1,3-dioxoprop-1-yl)-4-methylthio-benzoxazole.

4-chloro-5-(3-cyclopropyl-2-ethoxymethylene-1,3-dioxoprop-1-yl)-3-methoxybenzo[b]thiophene.

Reference Example 6

A solution of 5-(3-cyclopropyl-2-t-butyloxycarbonyl-1,3-dioxoprop-1-yl)-2,3-dihydrobenzo[b]furan (4.2g) in dry toluene was stirred at reflux with p-toluenesulphonic acid (0.2g) for 2 hours. The cooled solution was washed (sodium bicarbonate solution), then with water, dried (magnesium sulphate) and evaporated to give 5-(3-cyclopropyl-1,3-dioxoprop-1-yl)-2,3-dihydrobenzo[b]furan (2.9g) as an orange oil, NMR ($CDCl_3$) δ 0.9(2H,m), 1.15(2H,m), 1.65(1H,m), 3.15(2H,m), 4.55(2H,m), 6.15(1H,s), 6.75(1H,m), 7.7(2H,m), 16.3(1H,brs).

By proceeding in a similar manner the following compounds were prepared:

4-(3-cyclopropyl-1,3-dioxoprop-1-yl)-2,2-difluoro-1,3-benzodioxole, m.p. 46-47°C.

3-(3-cyclopropyl-1,3-dioxoprop-1-yl)-2-methylthiopyridine, NMR ($CDCl_3$) δ 0.9(2H,m), 1.15(2H,m), 1.7(1H,m), 2.5(3H,s), 6.15(1H,s), 7.15(1H,d), 7.75(1H,dd), 8.5(1H,dd), 16.0(1H,brs).

4-(3-cyclopropyl-1,3-dioxoprop-1-yl)-1-ethyl-3-trifluoromethylpyrazole, NMR ($CDCl_3$) δ 0.9(2H,m), 1.1(2H,m), 1.45(3H,t), 1.65(1H,m), 4.15(2H,q), 6.0(1H,s), 7.9(1H,s), 16.0(1H,brs).

3-chloro-2-(3-cyclopropyl-1,3-dioxoprop-1-yl)-5-trifluoromethylpyridine) m.p. 48-51°C.

2-t-butyl-4-chloro-7-(3-cyclopropyl-1,3-dioxoprop-1-yl)benzoxazole, as a yellow oil, NMR ($CDCl_3$) δ 1.1(2H,m), 1.55(9H,s), 1.85(1H,m), 6.7(1H,s), 7.4(1H,d), 7.95(1H,d), 16.3(1H,brs).

5-(3-cyclopropyl-1,3-dioxoprop-1-yl)-2,2-difluoro-4-methylthio-1,3-benzodioxole as an orange oil, NMR ($CDCl_3$) δ 1.01(2H,m), 1.22(2H,m), 1.75(1H,m), 2.57(3H,s), 6.01(1H,s), 6.97(1H,d), 7.32(1H,d).

7-(3-cyclopropyl-1,3-dioxoprop-1-yl)-4-fluoro-1,3-benzoxazol-2-one as an orange glass, NMR ($CDCl_3$) δ 0.85(2H,m), 1.0(2H,m),

1.71(1H,m), 2.85(1H,brs), 6.48(1H,s), 6.80(1H,t), 7.47(1H,m).

2-t-butyl-7-(3-cyclopropyl-1,3-dioxoprop-1-yl)-4-methylthio-benzoxazole as a yellow solid, NMR ($CDCl_3$) δ 1.05(2H,m), 1.25(2H,m), 1.57(9H,s), 1.88(1H,m), 2.67(3H,s), 6.70(1H,s), 7.16(1H,d), 7.92(1H,d).

5-(3-cyclopropyl-1,3-dioxoprop-1-yl)-1,3-benzodioxole as an orange oil, NMR ($CDCl_3$) δ 0.97(2H,m), 1.20(2H,m), 1.75(1H,m), 6.05(2H,s), 6.19(1H,s), 6.86(1H,d), 7.40(2H,m).

4-chloro-5-(3-cyclopropyl-1,3-dioxoprop-1-yl)-3-methoxybenzo[b]thiophene, NMR ($CDCl_3$) δ 1.02(2H,m), 1.23(2H,m), 1.76(1H,m), 3.96(3H,s), 6.14(1H,s), 6.46(1H,s), 7.46(1H,d), 7.66(1H,d).

5-(3-cyclopropyl-1,3-dioxoprop-1-yl)-4-methylthio-1,3-benzodioxole as an orange solid, NMR ($CDCl_3$) δ 1.0(2H,m), 1.2(2H,m), 1.7(1H,m), 2.5(3H,s), 6.0(1H,s), 6.1(2H,s), 6.7(1H,d), 7.1(1H,d).

4-(3-cyclopropyl-1,3-dioxoprop-1-yl)-1,3-benzodioxole

Reference Example 7

A stirred suspension of magnesium turnings (0.4g) in methanol (dry,) was treated with carbon tetrachloride to initiate the reaction and a solution of t-butyl 3-cyclopropyl-3-oxopropanoate (2.8g) in methanol (10 ml) added dropwise. The mixture was stirred at 60°C, then evaporated to dryness. Dry toluene was added and the solution re-evaporated. Another addition of dry toluene (50 ml) was made, followed by a suspension of 2,3-dihydrobenzo[b]furan-5-carboxylic acid chloride (2.76g) in dry toluene (20 ml). The resultant mixture was stirred at room temperature for 18 hours. Hydrochloric acid (2M) was added and the mixture stirred for 1 hour, separated and the organic phase washed with hydrochloric acid (2M), water, dried (magnesium sulphate) and evaporated to give 5-(3-cyclopropyl-2-t-butyloxycarbonyl-1,3-dioxoprop-1-yl)-2,3-dihydrobenzo[b]furan (4.2g) used directly in the next stage.

By proceeding in a similar manner the following compounds were prepared:

5-(3-cyclopropyl-2-t-butyloxycarbonyl-1,3-dioxoprop-1-yl)-1,3-benzodioxole.

4-(3-cyclopropyl-2-t-butyloxycarbonyl-1,3-dioxoprop-1-yl)-2,2-

difluoro-1,3-benzodioxole.

3-(3-cyclopropyl-2-t-butyloxycarbonyl-1,3-dioxoprop-1-yl)-2-methylthiopyridine.

4-(3-cyclopropyl-2-t-butyloxycarbonyl-1,3-dioxoprop-1-yl)-1-ethyl-3-trifluoromethylpyrazole.

2-t-butyl-4-chloro-7-(3-cyclopropyl-2-t-butyloxycarbonyl-1,3-dioxoprop-1-yl)benzoxazole.

5-(3-cyclopropyl-2-t-butyloxycarbonyl-1,3-dioxoprop-1-yl)-2,2-difluoro-4-methylthio-1,3-benzodioxole.

7-(cyclopropyl-2-t-butyloxycarbonyl-1,3-dioxoprop-1-yl)-4-fluoro-1,3-benzoxazol-2-one.

2-t-butyl-7-(3-cyclopropyl-2-t-butyloxycarbonyl-1,3-dioxoprop-1-yl)-4-methylthio-benzoxazole.

4-chloro-5-(3-cyclopropyl-2-t-butyloxycarbonyl-1,3-dioxoprop-1-yl)-3-methoxybenzo[b]thiophene.

3-chloro-2-(3-cyclopropyl-2-t-butyloxycarbonyl-1,3-dioxoprop-1-yl)-5-trifluoromethylpyridine.

5-(3-cyclopropyl-2-t-butyloxycarbonyl-1,3-dioxoprop-1-yl)-4-methylthio-1,3-benzodioxole.

4-(3-cyclopropyl-2-t-butyloxycarbonyl-1,3-dioxoprop-1-yl)-1,3-benzodioxole.

Reference Example 8

2,2-Difluoro-1,3-benzodioxole-4-carboxylic acid (15.0g) was dissolved in 1,2-dichloroethane and N,N-dimethylformamide and thionyl chloride (10.6g) added. The mixture was heated under reflux for 1 hour and the solvent evaporated in vacuo. The residue was dissolved in toluene and re-evaporated to yield 2,2-difluoro-1,3-benzodioxole-4-carboxylic acid chloride (17.35g).

By proceeding in a similar manner the following compounds were prepared:

1,2-dihydrobenzo[b]furan-5-carboxylic acid chloride.

1,3-benzodioxole-5-carboxylic acid chloride.

3-chloro-5-trifluoromethylpyridine-2-carboxylic acid chloride.

Reference Example 9

A mixture of 1-ethyl-3-trifluoromethylpyrazole-4-carboxylic acid (1.7g) and oxalyl chloride (0.78 ml) was stirred and heated at reflux with 1,2-dichloroethane (50 ml) and N, N-dimethylformamide

(4 drops). After 1 hour the mixture was evaporated in vacuo to give 1-ethyl-3-trifluoromethylpyrazole-4-carboxylic acid chloride (1.8g), used directly in the next stage.

By proceeding in a similar manner the following compounds were prepared:

2-t-butyl-4-chlorobenzoxazole-7-carboxylic acid chloride as an orange solid, used directly in the next stage.

2,2-difluoro-4-methylthio-1,3-benzodioxole-5-carboxylic acid chloride, obtained as an orange semi-solid.

4-fluoro-1,3-benzoxazol-2-one-7-carboxylic acid chloride, from the corresponding carboxylic acid [Synthetic Communications 20(10)m 1423(1990)] D.R. Reavill, S.K. Richardson.

2-t-butyl-4-methylthiobenzoxazole-7-carboxylic acid chloride.

2,3-dihydrobenzo[b]furan-5-carboxylic acid chloride.

1,3-benzodioxole-5-carboxylic acid chloride.

4-chloro-3-methoxybenzo[b]thiophene-5-carboxylic acid chloride.

Reference Example 10

n-Butyl lithium (11.6ml) of a 2.5M solution in hexanes) was added dropwise to a stirred solution of 2,2-difluoro-1,3-benzodioxole-5-carboxylic acid (2.8g) in dry tetrahydrofuran (75ml) maintained at -78°C under an inert atmosphere. After 6 hours at -78°C, a solution of dimethyl disulphide (3.75 ml) was added dropwise and the mixture left to reach room temperature overnight. Sodium hydroxide solution (2M) was added, the mixture washed with ether, acidified (hydrochloric acid) and the precipitated solid filtered. This was washed (hexane) and dried to give 2,2-difluoro-4-methylthio-1,3-benzodioxole-5-carboxylic acid (2.59g) a cream solid. A pure sample was obtained as colourless crystals m.p. 190-192°C by recrystallisation from toluene/cyclohexane.

By proceeding in a similar manner 4-methylthio-1,3-benzodioxole-5-carboxylic acid was prepared as a cream solid, m.p. 193 - 195°C.

Reference Example 11

A mixture of methyl 2-t-butyl-4-chloro-1,3-benzoxazole-7-carboxylate (5.7g) and sodium thiomethoxide (1.64g) in dry tetrahydrofuran (100 ml) was stirred at reflux for 48 hours. Water

was added and the mixture extracted with ether, washed (water), dried (magnesium sulphate) and evaporated. Purification by chromatography on silica gel, eluting with hexane/ethyl acetate (9:1) gave methyl 2-t-butyl-4-methylthio-1,3-benzoxazole-7-carboxylate (2,78g) as a cream solid, NMR ($CDCl_3$) δ 1.51(9H,s), 2.63(3H,s), 3.99(3H,s), 7.10(1H,d), 7.86(1H,d).

Reference Example 12

Oxalyl chloride (2.61 ml) and N,N-dimethylformamide (3 drops) was added to a stirred suspension of 2-t-butyl-4-chloro-1,3-benzoxazole-7-carboxylic acid (6.2g) and the mixture heated at reflux for 2 hours, cooled and evaporated. Dichloromethane was added and the solution added dropwise at 0°C to a stirred solution of methanol (3.05 ml) and triethylamine (10.2 ml) in dichloromethane. The mixture was stirred at room temperature for 18 hours, washed with hydrochloric acid (2M), water, sodium carbonate solution (50 ml) and water, then dried (magnesium sulphate) and evaporated to give methyl 2-t-butyl-4-chloro-1,3-benzoxazole-7-carboxylate (5.71g), as a light brown solid, m.p. 130-131°C.

Reference Example 13

n-Butyl lithium (101.6 ml of a 2.5M solution in hexane) was added during 30 minutes to a stirred solution of 2,5-dichloro-1-(trimethylacetylamino)benzene (25.0g) in dry tetrahydrofuran (250 ml) at -40°C, and the solution stirred at -20°C for 1.5 hours and poured onto solid carbon dioxide in dry tetrahydrofuran. The mixture was allowed to reach room temperature, 2M sodium hydroxide solution added and extracted with ethyl acetate. The aqueous solution was acidified (concentrated hydrochloric acid) and the precipitated solid collected and dried to give 2-t-butyl-4-chlorobenzoxazole-7-carboxylic acid (11.7g) m.p. 209-210°C.

Reference Example 14

To a stirred mixture of 2,5-dichloroaniline (15.0g), triethylamine (dry, 14.1 ml) and 4-dimethylaminopyridine (0.45g) in dry dichloromethane was added a solution of di-t-butyldicarbonate (22.2g) in dry dichloromethane. The mixture was stirred under nitrogen for 18 hours, and quenched by the addition of saturated ammonium chloride solution and extracted with dichloromethane.

The extract was dried (magnesium sulphate), evaporated and purified by chromatography on silica gel eluting with cyclohexane to give 2,5-dichloro-1-(trimethylacetylamino)benzene (12.2g) as a cream solid.

Reference Example 15

A mixture of methyl 4-chloro-3-methoxybenzo[b]thiophene-5-carboxylate (8.35g) and lithium hydroxide hydrate (1.37g) was stirred in methanol (75ml) and water (25ml) at room temperature for 4 days. The methanol was evaporated in vacuo and the mixture poured onto excess cold dilute hydrochloric acid. The solid was filtered, washed with cold cyclohexane and dried to give 4-chloro-3-methoxybenzo[b]thiophene-5-carboxylic acid (7.28g) as a white solid, NMR (d_6DMSO) δ 3.9(3H,s), 7.0(1H,s), 7.6(1H,d), 7.95(1H,d), 13.3(1H,brs).

Reference Example 16

Methanethiol gas (7.9g) was bubbled into a stirred suspension of sodium hydride (60% dispersion in oil; 6.0g) in dry dimethyl formamide with an exotherm of approximately 20°C observed. A solution of methyl 5-nitro-2-pyridinecarboxylate (23.8g) in dry dimethylformamide was added and the resulting suspension was stirred at 100°C for five hours then left to stand at room temperature overnight. The solvent was evaporated. Water was added cautiously to the residue and the resulting solution was neutralised by the addition of hydrochloric acid (2N) and extracted with ethyl acetate. The combined extracts were washed with water, dried (anhydrous sodium sulphate), filtered and evaporated. The residue was purified by column chromatography on silica eluted with a mixture of ethyl acetate and hexane to give two crude products. The first product was triturated in a mixture of cyclohexane and diethyl ether to yield methyl 5-methylthio-2-pyridinecarboxylate (5.78g) as a cream solid, m.p. 71-73°C. The second product was methyl 5-methoxy-2-pyridinecarboxylate (2.67g), obtained as a cream solid, m.p. 73-74°C.

Reference Example 17

A mixture of 5-nitropyridine-2-carboxylic acid (33.91g) and concentrated sulphuric acid (5 ml) in anhydrous methanol was heated at reflux for 20 hours. The solvent was evaporated and the

residue was taken up in dichloromethane and water. The organic layer was dried (anhydrous sodium sulphate), filtered and the solvent evaporated to yield methyl 5-nitropyridine-2-carboxylate (23.82g) as an orange solid, m.p. 156-159°C.

Reference Example 18

Diethyl 2-(5-nitropyridin-2-yl)malonate (67.47g) was stirred in water and aqueous sodium hydroxide solution (2N) was added followed by potassium permanganate (42g) causing the reaction temperature to rise to 60°C. Further portions of aqueous sodium hydroxide solution and potassium permanganate were added maintaining the reaction temperature at 60-70°C. After the final addition, the suspension was stirred at 60°C for 1.5 hours. The hot suspension was then filtered through 'Hyflo Supercel'. The filter cake was washed with aqueous sodium hydroxide solution (2N). On cooling to room temperature, the filtrate was carefully acidified to pH 1-2 with concentrated hydrochloric acid. The resulting precipitate was collected by filtration and dried to yield 5-nitropyridine-2-carboxylic acid (26.17g) as a fawn solid, m.p. 210-211°C.

By proceeding in a similar manner the following compound was prepared: 3-chloro-5-trifluoromethylpyridine-2-carboxylic acid (hydrochloride salt) m.p. > 139°C.

Reference Example 19

Diethyl malonate (74g) was added to a stirred suspension of sodium hydride (60% dispersion in oil; 18g) in dry tetrahydrofuran under an inert atmosphere. The resulting suspension was stirred at reflux for one hour. The mixture was cooled to 60°C and a solution of 2-chloro-5-nitropyridine (50g) in dry tetrahydrofuran was added. The resulting red solution was stirred at reflux for 3 hours then allowed to stand at room temperature overnight. The volume of solvent was reduced by evaporation, water was added to the residue and the mixture was acidified to pH 1 with concentrated hydrochloric acid. The mixture was extracted with ethyl acetate, washed with water, dried (anhydrous magnesium sulphate), filtered and evaporated. The crude product was triturated in a mixture of cyclohexane and diethyl ether to yield diethyl 2-(5-nitropyridin-2-yl)malonate (56.5g) as a yellow solid, m.p. 91.5-93.5°C.

By proceeding in a similar manner the following compound was prepared: diethyl 2-(3-chloro-5-trifluoromethylpyridin-2-yl)malonate b.p. 120-122°C (0.6-0.8 mbar).

Reference Example 20

Methyl cyclopropyl ketone (1.26g) was added to a stirred suspension of sodium hydride (60%, 0.6g) in dry ether. After 0.5 hours a solution of methyl 5-methylthiopyridine-2-carboxylate (1.9g) in dry ether was added and the mixture heated at reflux for 9 hours and left overnight at room temperature. Hydrochloric acid (2M, 50 ml) and ethyl acetate were added and the organic phase washed (water), dried (magnesium sulphate) and evaporated to give 2-(3-cyclopropyl-1,3-dioxoprop-1-yl)-5-methylthiopyridine (1.73g), m.p. 81-85°C.

Reference Example 21

Ethyl 1-ethyl-3-trifluoromethylpyrazole-4-carboxylate (2.17 g) was dissolved in ethanol and potassium hydroxide (1.06 g) in water was added. The reaction was stirred at room temperature overnight. Ethanol was removed under reduced pressure and the resulting residue partitioned between water and ether. The aqueous layer was separated, acidified with hydrochloric acid (2 M) and extracted with ether. The combined organic extracts were dried over anhydrous magnesium sulphate and evaporated in vacuo to give 1-ethyl-3-trifluoromethylpyrazole-4-carboxylic acid as a white solid (1.86 g). NMR ($CDCl_3$) δ 1.45(3H,t), 4.20(2H,q), 7.95(1H,s).

By proceeding in a similar manner the following compound was prepared:

2-t-butyl-4-methylthiobenzoxazole-7-carboxylic acid, m.p. 203-304°C.

Reference Example 22

Ethyl 3-trifluoromethylpyrazole-4-carboxylate (5 g), potassium carbonate (3.48 g) and ethyl iodide (2.3 ml) in acetonitrile were heated at reflux overnight. After cooling, ethyl acetate and water were added and the organic phase separated. The aqueous layer was extracted with ethyl acetate and the combined organic extracts were dried (magnesium sulphate) and evaporated under reduced pressure to give a yellow oil which was purified by crystallisation in hexane to produce 4-ethoxycarbonyl-1-ethyl-3-

trifluoromethylpyrazole as white crystals (3.65 g), 'H NMR ($CDCl_3$) δ 1.25(3H,t), 1.45(3H,t), 4.10(2H,q), 4.20(2H,q) 7.90(1H,s) ppm.

Reference Example 23

A mixture of 4-chloro-3-hydroxybenzo[b]thiophene-5-carboxylic acid (7.72g), caesium carbonate (24.2g), methyl iodide (42ml) and tetraethylammonium iodide (0.87g) was heated in acetonitrile at 50°C overnight. A further addition of methyl iodide (20 ml) was made, and heating at 50°C continued for 24 hours. The solvent was evaporated and the residue dissolved in ethyl acetate. The solution was washed with saturated sodium bicarbonate solution, water, dried over anhydrous magnesium sulphate, and evaporated in vacuo. The residue was purified by column chromatography eluting with ether/cyclohexane to yield methyl 4-chloro-3-methoxybenzo[b]thiophene-5-carboxylate (4.53g) as an oil, NMR ($CDCl_3$) δ 3.94 (6H, s), 6.43 (1H, s), 7.64 (2H, s).

Reference Example 24

A mixture of dimethyl 4-chloro-3-hydroxybenzo[b]thiophene-2,5-dicarboxylate (12.62g) and 2N sodium hydroxide was heated under reflux for 2 hours. The mixture was neutralised with 2N hydrochloric acid whilst still at 100°C. The solution was acidified with concentrated hydrochloric acid and stirred under reflux conditions for a further 30 minutes. A purple solid (7.72g) was filtered and dried in a dessicator and shown to be 4-chloro-3-hydroxybenzo[b]thiophene-5-carboxylic acid, NMR (DMSO D_6) 6.67 (1H, s), 7.54 (1H, d), 7.87 (1H, d), 10.3 (1H, s), 13.34 (1H, s) and 4.07 (2H, s), 7.63 (1H, d), 7.93 (1H, d), 13.34 (1H, s) (40% in the keto form).

Reference Example 25

Dimethyl 2,4-dichloro-isophthaloate (11.95g) and methyl thioglycolate (7.23g) was dissolved in N,N-dimethylformamide, and lithium hydroxide monohydrate (3.81g) added. The mixture was stirred at ambient temperature for 2 days, diluted with water and brought to pH 1 with hydrochloric acid. The solid was filtered, washed with boiling cyclohexane and dried by azeotropic removal of toluene to give dimethyl 4-chloro-3-hydroxybenzo[b]thiophene-2,5-dicarboxylate (13.44g) as a beige solid, m.p. 127-131°C.

Reference Example 26

2,4-Dichloro-3-methoxycarbonylbenzoylchloride (34.76g) was stirred and heated under reflux with methanol for 15 hours. After cooling, the solvent was evaporated and the residue recrystallised from cyclohexane to give dimethyl 2,4-dichloroisophthaloate (16.04g) as a beige solid, NMR (DMSO D_6) δ 3.87 (3H, s), 3.94 (3H, s), 7.74 (1H, d), 7.94 (1H, d).

Reference Example 27

2,4-Dichloro-3-methoxycarbonylbenzoic acid (32.37g) and thionyl chloride (100 ml) was heated under reflux with stirring for 3 hours. The mixture was cooled and evaporated in vacuo, then re-evaporated after addition of toluene to give 2,4-dichloro-3-methoxycarbonylbenzoyl chloride (34.76g) as a dark brown oil.

By proceeding in a similar manner but employing oxalyl chloride and a catalytic amount of DMF in dichloromethane in place of thionyl chloride the following compounds were prepared:

4-methylthio-1,3-benzodioxole-5-carboxylic acid chloride.

1,3-benzodioxole-4-carboxylic acid chloride.

Reference Example 28

To a stirred solution of diisopropylamine (22 ml) in dry tetrahydrofuran (160 ml) cooled to 0°C under an inert atmosphere was added n-butyl lithium (2.5M, 67 ml) dropwise. The solution was stirred for 30 minutes at 0°C, then added to a solution of methyl 2,6-dichlorobenzoate (26.62g) in dry tetrahydrofuran (160 ml) cooled to -78°C under an inert atmosphere. After 1.5 hours at this temperature the mixture was poured onto excess solid carbon dioxide and left to stand overnight. The solvent was evaporated in vacuo and the residue acidified with 2N hydrochloric acid. This was then extracted with ethyl acetate, dried over anhydrous magnesium sulphate and evaporated in vacuo to yield 2,4-dichloro-3-methoxycarbonylbenzoic acid (32.37g) as a solid, NMR (DMSO D_6) δ 3.93 (3H, s), 7.70 (1H, d), 7.91 (1H, d).

According to a feature of the present invention, there is provided a method for controlling the growth of weeds (i.e. undesired vegetation) at a locus which comprises applying to the locus a herbicidally effective amount of at least one 2-cyano-1,3-dione derivative of formula I or an enolic tautomeric

form thereof, or an agriculturally acceptable salt or metal complex thereof. For this purpose, the 2-cyano-1,3-dione derivatives are normally used in the form of herbicidal compositions (i.e. in association with compatible diluents or carriers and/or surface active agents suitable for use in herbicidal compositions), for example as hereinafter described.

The compounds of formula I show herbicidal activity against dicotyledonous (i.e. broad-leafed) and monocotyledonous (e.g. grass) weeds by pre- and/or, post-emergence application.

By the term "pre-emergence application" is meant application to the soil in which the weed seeds or seedlings are present before emergence of the weeds above the surface of the soil. By the term "post-emergence application" is meant application to the aerial or exposed portions of the weeds which have emerged above the surface of the soil. For example, the compounds of formula I may be used to control the growth of

* broad-leafed weeds, for example, Abutilon theophrasti, Amaranthus retroflexus, Bidens pilosa, Chenopodium album, Galium aparine, Ipomoea spp. e.g. Ipomoea purpurea, Sesbania exaltata, Sinapis arvensis, Solanum nigrum and Xanthium strumarium, and

* grass weeds, for example Alopecurus myosuroides, Avena fatua, Digitaria sanguinalis, Echinochloa crus-galli, Eleusine indica and Setaria spp, e.g. Setaria faberii or Setaria viridis, and

* sedges, for example, Cyperus esculentus.

The amounts of compounds of formula I applied vary with the nature of the weeds, the compositions used, the time of application, the climatic and edaphic conditions and (when used to control the growth of weeds in crop-growing areas) the nature of the crops. When applied to a crop-growing area, the rate of application should be sufficient to control the growth of weeds without causing substantial permanent damage to the crop. In general, taking these factors into account, application rates between 0.01 kg and 5 kg of active material per hectare give good results. However, it is to be understood that higher or lower application rates may be used, depending upon the particular problem of weed control

encountered.

The compounds of formula I may be used to control selectively the growth of weeds, for example to control the growth of those species hereinbefore mentioned, by pre- or post-emergence application in a directional or non-directional fashion, e.g. by directional or non-directional spraying, to a locus of weed infestation which is an area used, or to be used, for growing crops, for example cereals, e.g. wheat, barley, oats, maize and rice, soya beans, field and dwarf beans, peas, lucerne, cotton, peanuts, flax, onions, carrots, cabbage, oilseed rape, sunflower, sugar beet, and permanent or sown grassland before or after sowing of the crop or before or after emergence of the crop. For the selective control of weeds at a locus of weed infestation which is an area used, or to be used, for growing of crops, e.g. the crops hereinbefore mentioned, application rates between 0.01 kg and 4.0 kg, and preferably between 0.01 kg and 2 kg, of active material per hectare are particularly suitable.

The compounds of formula I may also be used to control the growth of weeds, especially those indicated above, by pre- or post-emergence application in established orchards and other tree-growing areas, for example forests, woods and parks, and plantations, e.g. sugar cane, oil palm and rubber plantations. For this purpose they may be applied in a directional or non- directional fashion (e.g. by directional or non-directional spraying) to the weeds or to the soil in which they are expected to appear, before or after planting of the trees or plantations at application rates between 0.25 kg and 5 kg, and preferably between 0.5 kg and 4 kg of active material per hectare.

The compounds of formula I may also be used to control the growth of weeds, especially those indicated above, at loci which are not crop-growing areas but in which the control of weeds is nevertheless desirable.

Examples of such non-crop-growing areas include airfields, industrial sites, railways, roadside verges, the verges of rivers, irrigation and other waterways, scrublands and fallow or uncultivated land, in particular where it is desired to control the growth of weeds in order to reduce fire risks. When used for such

purposes in which a total herbicidal effect is frequently desired, the active compounds are normally applied at dosage rates higher than those used in crop-growing areas as hereinbefore described. The precise dosage will depend upon the nature of the vegetation treated and the effect sought.

Pre- or post-emergence application, and preferably pre-emergence application, in a directional or non-directional fashion (e.g. by directional or non-directional spraying) at application rates between 1 kg and 20 kg, and preferably between 5 and 10 kg, of active material per hectare are particularly suitable for this purpose.

When used to control the growth of weeds by pre-emergence application, the compounds of formula I may be incorporated into the soil in which the weeds are expected to emerge. It will be appreciated that when the compounds of formula I are used to control the growth of weeds by post-emergence application, i.e. by application to the aerial or exposed portions of emerged weeds, the compounds of formula I will also normally come into contact with the soil and may also then exercise a pre-emergence control on later-germinating weeds in the soil.

Where especially prolonged weed control is required, the application of the compounds of formula I may be repeated if required.

According to a further feature of the present invention, there are provided compositions suitable for herbicidal use comprising one or more of the 2-cyano-1,3-dione derivatives of formula I or enolic tautomeric forms thereof, or agriculturally acceptable salts or metal complexes thereof in association with, and preferably homogeneously dispersed in, one or more compatible herbicidally-acceptable diluents or carriers and/or surface active agents [i.e. diluents or carriers and/or surface active agents of the type generally accepted in the art as being suitable for use in herbicidal compositions and which are compatible with compounds of formula I]. The term "homogeneously dispersed" is used to include compositions in which the compounds of formula I are dissolved in other components. The term "herbicidal compositions" is used in a broad sense to include not only compositions which are ready for

use as herbicides but also concentrates which must be diluted before use. Preferably, the compositions contain from 0.05 to 90% by weight of one or more compounds of formula I.

The herbicidal compositions may contain both a diluent or carrier and surface-active (e.g. wetting, dispersing, or emulsifying) agent. Surface-active agents which may be present in herbicidal compositions of the present invention may be of the ionic or non-ionic types, for example sulphoricinoleates, quaternary ammonium derivatives, products based on condensates of ethylene oxide with alkyl and polyaryl phenols, e.g. nonyl- or octyl-phenols, or carboxylic acid esters of anhydrosorbitols which have been rendered soluble by etherification of the free hydroxy groups by condensation with ethylene oxide, alkali and alkaline earth metal salts of sulphuric acid esters and sulphonic acids such as dinonyl- and dioctyl-sodium sulphonosuccinates and alkali and alkaline earth metal salts of high molecular weight sulphonic acid derivatives such as sodium and calcium lignosulphonates and sodium and calcium alkylbenzene sulphonates.

Suitably, the herbicidal compositions according to the present invention may comprise up to 10% by weight, e.g. from 0.05% to 10% by weight, of surface-active agent but, if desired, herbicidal compositions according to the present invention may comprise higher proportions of surface-active agent, for example up to 15% by weight in liquid emulsifiable suspension concentrates and up to 25% by weight in liquid water soluble concentrates.

Examples of suitable solid diluents or carriers are aluminium silicate, talc, calcined magnesia, kieselguhr, tricalcium phosphate, powdered cork, adsorbent carbon black and clays such as kaolin and bentonite. The solid compositions (which may take the form of dusts, granules or wettable powders) are preferably prepared by grinding the compounds of formula I with solid diluents or by impregnating the solid diluents or carriers with solutions of the compounds of formula I in volatile solvents, evaporating the solvents and, if necessary, grinding the products so as to obtain powders. Granular formulations may be prepared by absorbing the compounds of formula I (dissolved in suitable solvents, which may, if desired, be volatile) onto the solid diluents or carriers in granular

form and, if desired, evaporating the solvents, or by granulating compositions in powder form obtained as described above. Solid herbicidal compositions, particularly wettable powders and granules, may contain wetting or dispersing agents (for example of the types described above), which may also, when solid, serve as diluents or carriers.

Liquid compositions according to the invention may take the form of aqueous, organic or aqueous-organic solutions, suspensions and emulsions which may incorporate a surface-active agent. Suitable liquid diluents for incorporation in the liquid compositions include water, glycols, tetrahydrofurfuryl alcohol, acetophenone, cyclohexanone, isophorone, toluene, xylene, mineral, animal and vegetable oils and light aromatic and naphthenic fractions of petroleum (and mixtures of these diluents). Surface-active agents, which may be present in the liquid compositions, may be ionic or non-ionic (for example of the types described above) and may, when liquid, also serve as diluents or carriers.

Powders, dispersible granules and liquid compositions in the form of concentrates may be diluted with water or other suitable diluents, for example mineral or vegetable oils, particularly in the case of liquid concentrates in which the diluent or carrier is an oil, to give compositions ready for use.

When desired, liquid compositions of the compound of formula I may be used in the form of self-emulsifying concentrates containing the active substances dissolved in the emulsifying agents or in solvents containing emulsifying agents compatible with the active substances, the simple addition of water to such concentrates producing compositions ready for use.

Liquid concentrates in which the diluent or carrier is an oil may be used without further dilution using the electrostatic spray technique.

Herbicidal compositions according to the present invention may also contain, if desired, conventional adjuvants such as adhesives, protective colloids, thickeners, penetrating agents, stabilisers, sequestering agents, anti-caking agents, colouring agents and corrosion inhibitors. These adjuvants may also serve as carriers or diluents.

Unless otherwise specified, the following percentages are by weight. Preferred herbicidal compositions according to the present invention are

* aqueous suspension concentrates which comprise from 10 to 70% of one or more compounds of formula I, from 2 to 10% of surface-active agent, from 0.1 to 5% of thickener and from 15 to 87.9% of water,

* wettable powders which comprise from 10 to 90% of one or more compounds of formula I, from 2 to 10% of surface-active agent and from 8 to 88% of solid diluent or carrier,

* soluble powders which comprise from 10 to 90% of one or more compounds of formula I, from 2 to 40% of sodium carbonate and from 0 to 88% of solid diluent

* liquid water soluble concentrates which comprise from 5 to 50%, e.g. 10 to 30%, of one or more compounds of formula I, from 5 to 25% of surface-active agent and from 25 to 90%, e.g. 45 to 85%, of water miscible solvent, e.g. dimethylformamide, or a mixture of water-miscible solvent and water,

* liquid emulsifiable suspension concentrates which comprise from 10 to 70% of one or more compounds of formula I, from 5 to 15% of surface-active agent, from 0.1 to 5% of thickener and from 10 to 84.9% of organic solvent

* granules which comprise from 1 to 90%, e.g. 2 to 10% of one or more compounds of formula I, from 0.5 to 7%, e.g. 0.5 to 2%, of surface-active agent and from 3 to 98.5%, e.g. 88 to 97.5%, of granular carrier and,

* emulsifiable concentrates which comprise 0.05 to 90%, and preferably from 1 to 60% of one or more compounds of formula I, from 0.01 to 10%, and preferably from 1 to 10%, of surface-active agent and from 9.99 to 99.94%, and preferably from 39 to 98.99%, of organic solvent.

Herbicidal compositions according to the present invention may also comprise the compounds of formula I in association with, and preferably homogeneously dispersed in, one or more other pesticidally active compounds and, if desired, one or more compatible pesticidally acceptable diluents or carriers, surface-active agents and conventional adjuvants as hereinbefore

described. Examples of other pesticidally active compounds which may be included in, or used in conjunction with, the herbicidal compositions of the present invention include herbicides, for example to increase the range of weed species controlled for example alachlor [2-chloro-2,6'-diethyl-N-(methoxy-methyl)-acetanilide], atrazine [2-chloro-4-ethylamino-6-isopropylamino-1,3,5-triazine], bromoxynil [3,5-dibromo-4-hydroxybenzonitrile], chlortoluron [N'-(3-chloro-4-methylphenyl)-N,N-dimethylurea], cyanazine [2-chloro-4-(1-cyano-1- methylethylamino)-6-ethylamino-1,3,5-triazine], 2,4-D [2,4-dichlorophenoxy-acetic acid], dicamba [3,6-dichloro-2-methoxybenzoic acid], difenzoquat [1,2- dimethyl-3,5-diphenyl-pyrazolium salts], flampropmethyl [methyl N-2-(N-benzoyl-3-chloro-4-fluoroanilino)-propionate], fluometuron [N'-(3-trifluoro- methylphenyl)-N,N-dimethylurea], isoproturon [N'-(4-isopropylphenyl)-N,N-dimethylurea], nicosulfuron [2-(4,6-dimethoxypyrimidin-2-ylcarbamoylsulfamoyl)-N,N-dimethylnicotinamide] insecticides, e.g. synthetic pyrethroids, e.g. permethrin and cypermethrin, and fungicides, e.g. carbamates, e.g. methyl N-(1-butyl-carbamoyl- benzimidazol-2-yl)carbamate, and triazoles e.g. 1-(4-chloro-phenoxy)-3,3- dimethyl-1-(1,2,4-triazol-1-yl)-butan-2-one.

Pesticidally active compounds and other biologically active materials which may be included in, or used in conjunction with, the herbicidal compositions of the present invention, for example those hereinbefore mentioned, and which are acids, may, if desired, be utilized in the form of conventional derivatives, for example alkali metal and amine salts and esters.

According to a further feature of the present invention there is provided an article of manufacture comprising at least one of the 2-cyano-1,3-dione derivatives of formula I or an agriculturally-acceptable salt thereof or, as is preferred, a herbicidal composition as hereinbefore described, and preferably a herbicidal concentrate which must be diluted before use, comprising at least one of the 2-cyano-1,3-dione derivatives of formula I within a container for the aforesaid derivative or derivatives of formula I, or a said herbicidal composition, and instructions physically associated with the

aforesaid container setting out the manner in which the aforesaid derivative or derivatives of formula I or herbicidal composition contained therein is to be used to control the growth of weeds. The containers will normally be of the types conventionally used for the storage of chemical substances which are solid at normal ambient temperatures and herbicidal compositions particularly in the form of concentrates, for example cans and drums of metal, which may be internally lacquered, and plastics materials, bottles or glass and plastics materials and, when the contents of the container is a solid, for example granular, herbicidal compositions, boxes, for example of cardboard, plastics materials and metal, or sacks. The containers will normally be of sufficient capacity to contain amounts of the 2-cyano-1,3-dione derivative or herbicidal compositions sufficient to treat at least one acre of ground to control the growth of weeds therein but will not exceed a size which is convenient for conventional methods of handling. The instructions will be physically associated with the container, for example by being printed directly thereon or on a label or tag affixed thereto. The directions will normally indicate that the contents of the container, after dilution if necessary, are to be applied to control the growth of weeds at rates of application between 0.01 kg and 20 kg of active material per hectare in the manner and for the purposes hereinbefore described.

The following Examples illustrate herbicidal compositions according to the present invention:

EXAMPLE C1

A soluble concentrate is formed from :

Active ingredient (compound 1)	20% w/v
Potassium hydroxide solution 33% w/v	10% v/v
Tetrahydrofurfuryl alcohol (THFA)	10% v/v
Water	to 100 volumes.

by stirring THFA, active ingredient (compound 1) and 90% volume of water and slowly adding the potassium hydroxide solution until a steady pH 7-8 was obtained then making up to volume with water.

Similar soluble concenttrates may be prepared as described above by replacing the 2-cyano-1,3-dione (compound 1) by other compounds of formula (I).

EXAMPLE C2

A wettable powder is formed from :

Active ingredient (compound 1)	50%	w/w
Sodium dodecylbenzene sulphonate	3%	w/w
Sodium lignosulphate	5%	w/w
Sodium formaldehyde alkylnaphthalene sulphonate	2%	w/w
Microfine silicon dioxide	3%	w/w and
China clay	37%	w/w

by blending the above ingredients together and grinding the mixture in an air jet mill.

Similar wettable powders may be prepared as described above by replacing the 2-cyano-1,3-dione (compound 1) by other compounds of formula I.

EXAMPLE C3

An aqueous suspension concentrate is formed from:

* active ingredient (compound 1):	50% w/v
* nonylphenol/ethylene oxide condensate containing 9 moles ofethylene oxide per mol of phenol:	1 % w/v
* sodium salt of polycarboxylic acid:	0.2% w/v
* Ethylene glycol :	5% w/v
* polysaccaride xanthan gum thickener:	0.15% w/v
* water to	100% by volume

by intimately mixing the ingredients and grinding in a ball-mill for 24 hours.

Similar aqueous concentrates may be prepared as described above by replacing the 2-cyano-1,3-dione (compound 1) by other compounds of formula (I).

Representative compounds of formula (I) have been used in herbicidal applications according to the following procedures.

METHOD OF USE OF HERBICIDAL COMPOUNDS:

a) General

Appropriate quantities of the compounds used to treat the plants were dissolved in acetone to give solutions equivalent to application rates up to 4000g test compound per hectare (g/ha). These solutions were applied from a standard laboratory herbicide sprayer delivering the equivalent of 290 litres of spray fluid per hectare.

b) Weed control : Pre-emergence

The seeds were sown in 70 mm square, 75 mm deep plastic pots in non-sterile soil . The quantities of seed per pot were as follows:-

Weed species	Approx number of seeds/pot
1) Broad-leafed weeds	
Abutilon theophrasti	10
Amaranthus retroflexus	20
Galium aparine	10
Ipomoea purpurea	10
Sinapis arvensis	15
Xanthium strumarium	2.
2) Grass weeds	
Alopecurus myosuroides	15
Avena fatua	10
Echinochloa crus-galli	15
Setaria viridis	20.
3) Sedges	
Cyperus esculentus	3.
Crop	
1) Broad-leafed	
Cotton	3
Soya	3.
2) Grass	
Maize	2
Rice	6

Wheat 6.

The compounds of the invention were applied to the soil surface, containing the seeds, as described in (a). A single pot of each crop and each weed was allocated to each treatment, with unsprayed controls and controls sprayed with acetone alone.

After treatment the pots were placed on capillary matting kept in a glass house, and watered overhead . Visual assessment of crop damage was made 20-24 days after spraying. The results were expressed as the percentage reduction in growth or damage to the crop or weeds, in comparison with the plants in the control pots.

c) Weed control : Post-emergence

The weeds and crops were sown directly into John Innes potting compost in 75 mm deep, 70 mm square pots except for Amaranthus which was pricked out at the seedling stage and transferred to the pots one week before spraying. The plants were then grown in the greenhouse until ready for spraying with the compounds used to treat the plants. The number of plants per pot were as follows :-

1) Broad leafed weeds

Weed species	Number of plants per pot	Growth stage
Abutilon theophrasti	3	1-2 leaves
Amaranthus retroflexus	4	1-2 leaves
Galium aparine	3	1st whorl
Ipomoea purpurea	3	1-2 leaves
Sinapis arvensis	4	2 leaves
Xanthium strumarium	1	2-3 leaves.

2) Grass weeds

Weed species	Number of plants per pot	Growth stage
Alopecurus myosuroides	8-12	1-2 leaves
Avena fatua	12-18	1-2 leaves
Echinochloa crus-galli	4	2-3 leaves
Setaria viridis	15-25	1-2 leaves.

3) Sedges

Weed species	Number of plants per pot	Growth stage
Cyperus esculentus	3	3 leaves.

1) Broad leafed

Crops	Number of plants per pot	Growth stage
Cotton	2	1 leaf
Soya	2	2 leaves.

2) Grass

Crops	Number of plants per pot	Growth stage
Maize	2	2-3 leaves
Rice	4	2-3 leaves
Wheat	5	2-3 leaves.

The compounds used to treat the plants were applied to the plants as described in (a). A single pot of each crop and weed species was allocated to each treatment, with unsprayed controls and controls sprayed with acetone alone.

After treatment the pots were placed on capillary matting in a glass house, and watered overhead once after 24 hours and then by controlled sub-irrigation. Visual assessment of crop damage and weed control was made 20-24 days after spraying. The results were expressed as the percentage reduction in growth or damage to the crop or weeds, in comparison with the plants in the control pots.

When applied either pre or post- emergence at 4 kg/ha or less, compounds 1 to 15 gave at least 90% control of one or more weed species.

When applied post-emergence at a dose rate of 1kg/ha or less, compounds 1, 2, 3, 4, 5, 8, 9, 10, 11, 12, 13 and 14 gave at least 90% control of Echinochloa crus-galli.

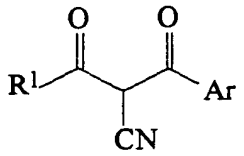
When applied post-emergence at a dose rate of 250g/ha or less, compounds 2, 3, 4, 5, 8, 10, 13 and 14 gave at least 90% control of Echinochloa crus-galli.

When applied post-emergence at a dose rate of 1 kg/ha or less, compounds 3, 7, 8, 9,10, 13, 14 and 15 gave at least 90% control of Amaranthus retroflexus.

When applied pre-emergence at a dose rate of 1 kg/ha or less, compounds 3, 4, 6, 8, 9, 10, 13 and 14 gave at least 80% control of Amaranthus retroflexus.

CLAIMS

1. A 2-cyano-1,3-dione derivative of formula I:



(I)

wherein:

Ar represents a monocyclic or fused bicyclic heterocyclic system Het having a heterocyclic first ring and an optional second heterocyclic or carbocyclic ring, the second ring when present being fused to the first ring, the first ring having from 1 to 4 hetero ring atoms and from 4 to 7 total ring atoms, the first ring being aromatic or non-aromatic and being optionally substituted by from 1 to 4 R^2 groups which may be the same or different, the second ring being optionally substituted by from 1 to 4 R^2 groups which may be the same or different;

R^1 represents a cycloalkyl group containing from three to six carbon atoms optionally substituted by one or more groups selected from R^4, $-CO_2R^4$, $-SR^4$, halogen and $-OR^4$;

R^2 represents:-

a halogen atom,

a straight- or branched- chain alkyl group containing from one to six carbon atoms which is substituted by a group $-OR^4$; or

a group selected from -OH, R^4, $-SR^5$, $-SOR^5$, $-SO_2R^5$, $-O-SO_2R^5$, $-CO_2R^4$, $-COR^4$, $-OR^5$, $-NR^6R^7$, $-N(R^8)SO_2R^5$, nitro, cyano, $-O(CH_2)_m-OR^4$, $-(-CR^9R^{10}-)_t-S(O)_pR^5$ and $-NR^{11}R^{12}$;

when the first and/or second ring of Het is non-aromatic, then R^2 may also represent =O, =S, cyclic ketal or cyclic thioketal;

R^4 represents a straight- or branched- chain alkyl group containing from one to six carbon atoms which is optionally substituted by one or more halogen atoms;

R^5 represents:-

a group R^4 or

phenyl optionally substituted by from one to five groups selected from halogen, R^4, $-CO_2R^4$, $-COR^4$, $-OR^4$, nitro, cyano and

$-O(CH_2)_m-OR^4$;

R^6 and R^7, which may be the same or different, each represent the hydrogen atom or a straight- or branched- chain alkyl group containing from one to six carbon atoms which is optionally substituted by one or more halogen atoms;

m represents an integer from one to three;

R^8 represents:-

the hydrogen atom;

a straight- or branched-chain alkyl, alkenyl or alkynyl group containing up to ten carbon atoms which is optionally substituted by one or more halogen atoms;

R^9 and R^{10}, which may be the same or different, each represents:

the hydrogen atom; a straight- or branched-chain alkyl group containing up to 6 carbon atoms which is optionally substituted by one or more halogen atoms; or phenyl optionally substituted by from one to five groups which may be the same or different selected from halogen, R^4, $-CO_2R^4$, $-COR^4$, $-OR^4$, nitro, cyano and $-O(CH_2)_m-OR^4$;

p is zero, 1 or 2; t represents an integer from one to three;

R^{11} represents $-COR^4$ or $-CO_2R^4$;

R^{12} represents:-

the hydrogen atom;

a straight- or branched- chain alkyl group containing up to six carbon atoms optionally substituted by one or more halogen atoms;

or a cycloalkyl group containing from three to six carbon atoms;

an enolic tautomeric form thereof,

or an agriculturally acceptable salt or metal complex thereof.

2. A compound according to claim 1 wherein R^1 represents a cyclopropyl group optionally substituted by a group R^4, wherein R^4 is alkyl.

3. A compound according to claim 1 or 2 in which Ar represents an optionally substituted fused bicyclic heterocyclic system having a heterocyclic first ring and a second carbocyclic ring

are preferred.

4. A compound according to claim 1, 2 or 3 in which Ar represents optionally substituted 1,3-benzodioxole, benzo[b]thiophene, benzoxazolinone, benzoxazole or benzo[b]furan.

5. A compound according to claim 1 or 2 in which Ar represents optionally substituted pyridyl, pyrazolyl or thienyl.

6. A compound according to any one of claims 1 to 5 in which Ar represents a group Het which is optionally substituted by from one to three groups R^2

7. A compound according to claim in which R^2 represents a halogen atom or a group selected from $-SR^5$, $-SOR^5$, $-SO_2R^5$, $-CH_2S(O)_pR^5$, $-CO_2R^4$ and $-OR^5$.

8. A compound according to claim 1 which is:

2-cyano-3-cyclopropyl-1-(2,2-difluoro-1,3-benzodioxol-4-yl)propan-1,3-dione;

1-(2-t-butyl-4-chlorobenzoxazol-7-yl)-2-cyano-3-cyclopropylpropan-1,3-dione;

2-cyano-3-cyclopropyl-1-(2,2-difluoro-4-methylsulphonyl-1,3-benzodioxol-5-yl)propan-1,3-dione;

2-cyano-3-cyclopropyl-1-(4-fluoro-3-methyl-1,3-benzoxazolin-2-one-7-yl)propan-1,3-dione;

1-(2-t-butyl-4-methylthiobenzoxazol-7-yl)-2-cyano-3-cyclopropylpropan-1,3-dione;

2-cyano-3-cyclopropyl-1-(2,3-dihydrobenzo[b]furan-5-yl)propan-1,3-dione;

2-cyano-3-cyclopropyl-1-(1,3-benzodioxol-5-yl)propan-1,3-dione;

1-(4-chloro-3-methoxybenzo[b]thien-5-yl)-2-cyano-3-cyclopropylpropan-1,3-dione;

2-cyano-3-cyclopropyl-1-(5-methylthiopyrid-2-yl)propan-1,3-dione;

1-(3-chloro-5-trifluoromethylpyrid-2-yl)-2-cyano-3-cyclopropylpropan-1,3-dione;

2-cyano-3-cyclopropyl-1-(2-methylthiopyrid-3-yl)propan-1,3-dione;

2-cyano-3-cyclopropyl-1-(1-ethyl-3-trifluoromethyl-pyrazol-4-yl)propan-1,3-dione;

2-cyano-3-cyclopropyl-1-(4-methylsulphonyl-1,3-benzodioxol-5-yl)propan-1,3-dione;

2-cyano-3-cyclopropyl-1-(4-methylthio-1,3-benzodioxol-5-yl)propan-1,3-dione; or

(1,3-benzodioxol-4-yl)-2-cyano-3-cyclopropylpropan-1,3-dione;

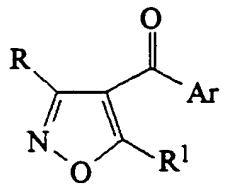
an enolic tautomeric form thereof,

or an agriculturally acceptable salt or metal complex thereof.

9. A herbicidal composition comprising an effective amount of a compound according to any one of claims 1 to 8 or an enolic tautomeric form thereof, or an agriculturally acceptable salt or metal complex thereof in association with an agriculturally acceptable diluent or carrier and/or surface active agent.

10. A method for the control of weeds at a locus which comprises applying to said locus an effective amount of a compound according to any one of claims 1 to 8 or an enolic tautomeric form thereof, or an agriculturally acceptable salt or metal complex thereof.

11. A process for the preparation of a 2-cyano-1,3-dione derivative of formula I as defined in claim 1 which comprises the reaction of a compound of formula(II):



(II)

wherein R^1 and Ar are as defined in claim 1 and R represents the hydrogen atom or an ester, with a base;

optionally followed by the conversion of the compound thus obtained into an agriculturally acceptable salt or metal complex thereof.

12. A process for the preparation of a 2-cyano-1,3-dione derivative of formula I as defined in claim 1 which comprises:

(a) reacting an acid chloride of formula ArC(O)Cl, wherein Ar is as defined in claim 1, with a beta-ketonitrile of formula $R^1C(O)CH_2CN$, wherein R^1 is as defined in claim 1;

(b) reacting an acid chloride of formula R^1COCl, wherein R^1 is as defined in claim 1, with a beta-ketonitrile of formula $ArC(O)CH_2CN$, wherein Ar is as defined in claim 1;

(c) where R^2 represents $-SOR^5$ or $-SO_2R^5$; oxidising the sulphur atom of the corresponding compound of formula (I) in which R^2 represents $-SR^5$ or $-SOR^5$;

(d) where a ring member of the group Het is -SO- or $-SO_2-$, oxidising the ring sulphur atom of the corresponding compound of formula (I);

optionally followed by the conversion of the compound thus obtained into an agriculturally acceptable salt or metal complex thereof.

INTERNATIONAL SEARCH REPORT

Inter nal Application No
PCT/EP 95/00950

A. CLASSIFICATION OF SUBJECT MATTER
IPC 6 C07D263/56 A01N43/76 C07D317/46 A01N43/30 C07D263/58
C07D277/64 A01N43/78 C07D307/79 C07D317/54 C07D333/64
C07D213/70 C07D213/61 C07D231/12

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 6 C07D A01N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	EP,A,0 213 892 (ROHM & HAAS) 11 March 1987 cited in the application see claim 1	1-12
A	EP,A,0 496 631 (RHONE-POULENC AGRICULTURE) 29 July 1992 cited in the application see claim 1	1-12
A	EP,A,0 496 630 (ROHM & HAAS AGRICULTURE) 29 July 1992 cited in the application see claim 1	1-12
A	EP,A,0 326 108 (BRISTOL-MYERS) 2 August 1989 Page 5, formula (IX)	1-8

-/--

[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

° Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
13 June 1995	30. 06. 95

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax (+31-70) 340-3016	Gettins, M

Form PCT/ISA/210 (second sheet) (July 1992)

INTERNATIONAL SEARCH REPORT

Inter nal Application No
PCT/EP 95/00950

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	EP,A,0 326 107 (BRISTOL-MYERS) 2 August 1989 Figure (XIII) on page 5	1-8

Form PCT/ISA/210 (continuation of second sheet) (July 1992)

INTERNATIONAL SEARCH REPORT

...nformation on patent family members

Inter nal Application No
PCT/EP 95/00950

Patent document cited in search report	Publication date	Patent family member(s)		Publication date
EP-A-213892	11-03-87	US-A-	4781750	01-11-88
		AU-A-	6118486	05-03-87
		DE-A-	3684535	30-04-92
		EP-A-	0213707	11-03-87
		JP-A-	62084040	17-04-87
EP-A-496631	29-07-92	AU-B-	647875	31-03-94
		AU-A-	1042092	30-07-92
		BG-A-	95818	31-03-94
		CN-A-	1063682	19-08-92
		JP-A-	5004960	14-01-93
		NZ-A-	241375	25-02-94
		OA-A-	9533	15-11-92
EP-A-496630	29-07-92	AU-B-	647874	31-03-94
		AU-A-	1041992	30-07-92
		BG-A-	95817	31-03-94
		CN-A-	1066843	09-12-92
		JP-A-	4312565	04-11-92
		NZ-A-	241376	25-02-94
		OA-A-	9532	15-11-92
EP-A-326108	02-08-89	US-A-	4935434	19-06-90
		JP-A-	1242577	27-09-89
		JP-C-	1790821	29-09-93
		JP-B-	4076989	07-12-92
EP-A-326107	02-08-89	US-A-	4888357	19-12-89
		CA-A-	1314562	16-03-93
		JP-A-	2001451	05-01-90